# Aspects of Vitamin A

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# Aspects of Vitamin A

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## SUMMARY

Musgrave Park Hospital in 1942 was the site of an Anglo-American Vitamin A caper. A threatened court-martial was pre-empted. Subsequently the Queen's lecturer in Anatomy, JW Millen, who was the other lecturer to the first editor of this journal, RH Hunter, did much distinguished work. The neurological effects of Vitamin A were elucidated. Further work on cerebrospinal fluid (CSF), placenta, thalidomide and poliomyelitis led to the pre-eminence in applied anatomy and teratology of now Reader James Wilson Millen and Professors JD Boyd and WJ Hamilton, all Queen's Medical School graduates. Training of RH Hunter, JH Biggart and JD Boyd at Johns Hopkins University profoundly influenced these seminal discoveries. The Garretts, a family of Lisburn, County Down origin, saved Johns Hopkins Hospital and Medical School from financial disaster. The Garretts founded a commercial and mercantile empire that took control of the Baltimore and Ohio (B and O) Railroad and enabled the Garretts to dictate that women should be admitted to the Hopkins Medical School and Hospital on exactly the same terms as men. All women and men should already be university honours graduates. Winston S Churchill on his progress up and down the B and O main line in March 1946, recounted to President Harry S Truman and Harry Hopkins his mother's tales of the Garrett boys' adventures.


**Key words:** Hydrocephalus, Poliomyelitis, Teratology

## INTRODUCTION

As a Christmas present in 1941, I* received from my parents a copy of *British Medicine*[1], which cost 3s 6d. I was told it might be taken back on Boxing Day for the Yanks. A fortnight before, Hitler had declared war on the United States. Benjamin Rycroft, since November my brother's godfather[2], was frequently in Windy Ridge, our rented Dunmurry Lane house. Ben read my temporary Christmas present with me. He was horrified when we reached pages 42 and 43 where the discovery of vitamins A and D is ascribed solely to Gowland Hopkins and the Mellanbys[1]. Ben told me that this simply was not true—a Kansan Hopkins Professor of Biochemistry had made these discoveries[3-6]. Moreover, he had been appointed to the Section on Research of the US National Conference on Nutrition in Defense, which advised the lend-lease program[7]. "He was not mean like Sir Edward Mellanby[8] who controlled lots of money and would not give any away, not even to make the penicillin which had run out for your pneumonia" [9].

My father, Angus, was confronted by Ben in my presence. Ben said the book was "ill-informed and provocative". "Maybe", said my father, but it should go back to Musgrave Park to show the Harvard doctors that they must educate and treat with tact those divided by a common language[10].

* All first-person references in this paper are to the first author.

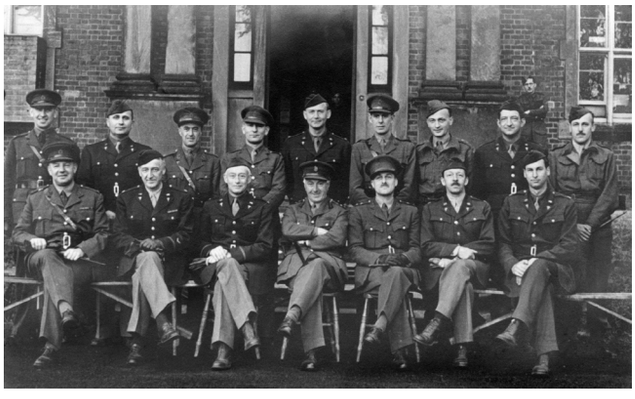

*Fig 1*. The 31st British General Hospital and US 5th General (Harvard) Hospital combined senior staff physicians and surgeons at the time of the vitamin A caper just before the epidemic traced to contaminated US yellow fever vaccine. Angus Hedley-Whyte, Commanding Officer 31st, and Professor Thomas Lanman, Chief surgeon 5th and Professor Theodore (Ted) Badger, chief of Medicine, 5th [10], are in the front row. Benjamin Rycroft, later knighted[2,9], is in the back row. *Photo courtesy of Col Magnus Smedal, Head of Radiology, 5th General Hospital, gift to John Hedley-Whyte*.

The book was repossessed and was replaced with a crash helmet. Hugh Cairns was insisting that every military motor-bike rider wear one[11]. I was not allowed to drive my pony and trap unless I was wearing the helmet firmly strapped up.

In March 1942, Ted Badger (Fig. 1) arrived from Harvard to be chief of Medicine at Musgrave Park for Harvard's Fifth General Hospital[10]. He read *British Medicine* which was now in "Hut 1" (Officers), Musgrave Park, Belfast. Ted had graduated from Yale. As a tuberculosis specialist and a Boston City Hospital disciple of Max Finland[9], he knew all about Elmer McCollum, PhD, Yale, 1904 (Fig. 2), and the Hopkinses, both Johns and Gowland (Fig. 3). Moreover, he had sailed a small boat across the Atlantic and knew all about nutrition.

Then started the food wars and the intrusive behaviour of the US and UK authorities. The enforcers were chiefly US

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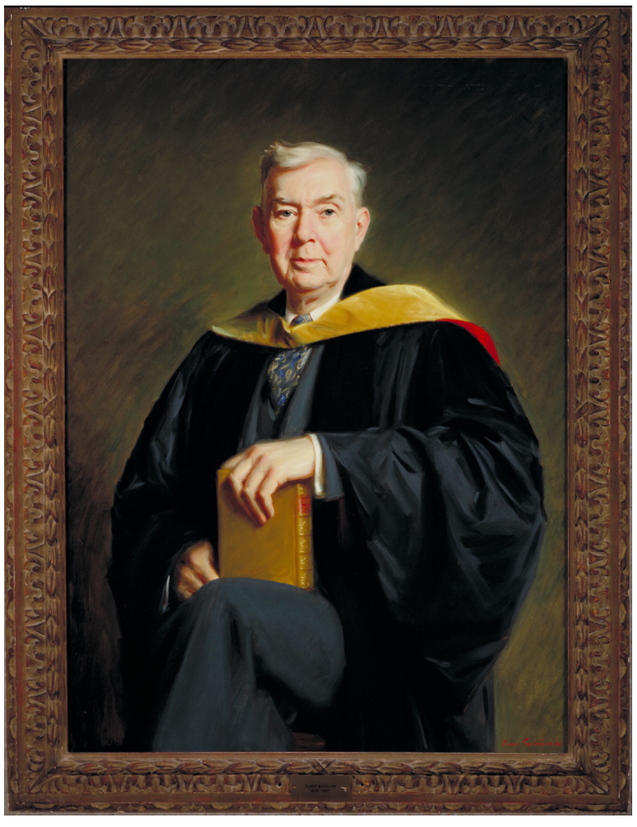

*Fig 2*. Elmer V McCollum by Paul Trebilcock, oil on canvas, 1954. Courtesy of the Alan Mason Chesney Medical Archives of the Johns Hopkins Medical Institutions, photograph by Aaron Levin. Professor Elmer Verner McCollum, PhD, ScD, LLD, DHL, NAS, FRS (1879-1967), was the discoverer together with Marguerite Davis, of Vitamin A[3-6]. Later McCollum discovered Vitamin D[6,12-15]. Born of an illiterate mother in a rural Kansas pioneer family, McCollum initially supported himself, his parents and siblings by becoming a lamp lighter in Lawrence, Kansas. On this regime, lights were lit at dusk and doused at 1:30 am. McCollum developed techniques so that he could become an analyst of wild-cat Kansas oil. His father developed tuberculosis of the spine, but despite these misfortunes, his mother was taught to read and write and all five children graduated from University[7,16,17]. Having obtained a BA and MA from the University of Kansas, Elmer was called to Yale to pursue a PhD in Nutrition. In 1917, having already discovered Vitamin A, while he was on the faculty at the University of Wisconsin, he was appointed Professor of Chemical Hygiene at Johns Hopkins: later his chair was changed to Biochemistry. McCollum served Johns Hopkins from 1917 until his death in 1967. He was elected to the National Academy of Sciences of the United States in 1920[16] and to an FRS in 1961[17]. McCollum succeeded William H Welch[18] as senior mentor of young researchers in the biological sciences at Johns Hopkins. In 1921, at Hopkins, McCollum sponsored the Herter Lecture of Frederick Gowland Hopkins MD, DSc, FRS of Cambridge University[19]. Subsequently McCollum taught Dicky Hunter[20], JH Biggart[21] and JD Boyd[22] from Queen's.

military policemen with bemused sporadic cooperation by the Garda on both sides of the Éire border[28]. British regiments were given considerable latitude in what foods they procured within a certain supplementable budget. Food from Éire and near the border was effectively proscribed for British troops

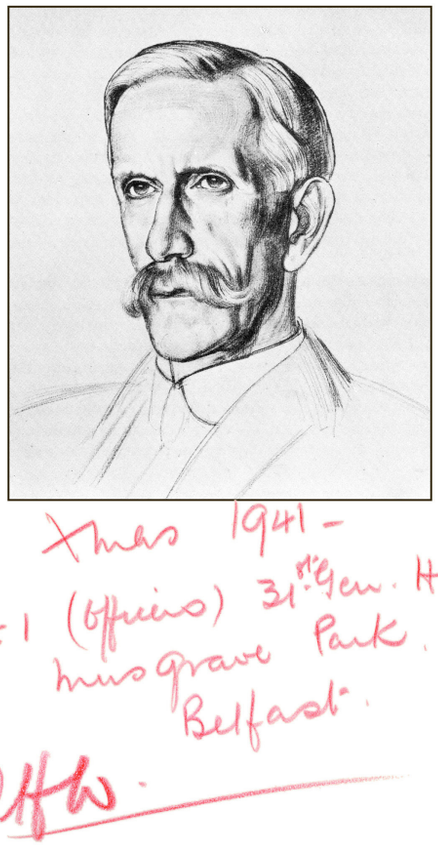

*Fig 3*. Sir Frederick Gowland Hopkins, OM, MD, FRS. Drawing by Eric Kennington, reproduced by permission of the Master and Fellows of Trinity College, Cambridge[1]. "Hoppy" was the first Professor of Biochemistry at Cambridge, Herter Lecturer, Johns Hopkins 1921, 1929 Nobel Laureate together with Professor Eijkman[19,23]. GM Trevelyan said of Hopkins, "He only thought of others. And so he was loved no less than he was admired"[24]. Hopkins' Department included JBS Haldane (1923-32), Joseph and Dorothy Needham and FJW Roughton[19,24,25]. The Massachusetts General Hospital called FJW Roughton to Harvard to aid with muscle physiology during prolonged cardio-pulmonary bypass[26,27]. My father's inscription is reproduced from the frontspiece of my "temporary" present[1].

- the rationale was that the Nazis, having allegedly infiltrated Éire, would poison Ulster - preferably starting with a "soft" target. The American forces were even stricter. Wherever possible, American forces were to be given only American food[29,30]. The U-boats in 1942 prevented this, but my sister and I were fed bananas by the Harvard doctors and nurses—our first memories of a banana or a tangerine.

## VITAMIN A

My father was, in spring 1942, charged as commanding officer of Musgrave Park with contravening the UK food regulations. He was sent an Official Letter of Reprimand. A court-martial was threatened. This gambit did not please the Musgrave Park physicians. Rycroft and his good friend and fellow zoo consultant, Dicky Hunter[9] launched the Vitamin A reprisal. They tested patients and physicians for night-blindness and looked at the records of many previous tests. Not surprisingly, quite a few cases were found. It was

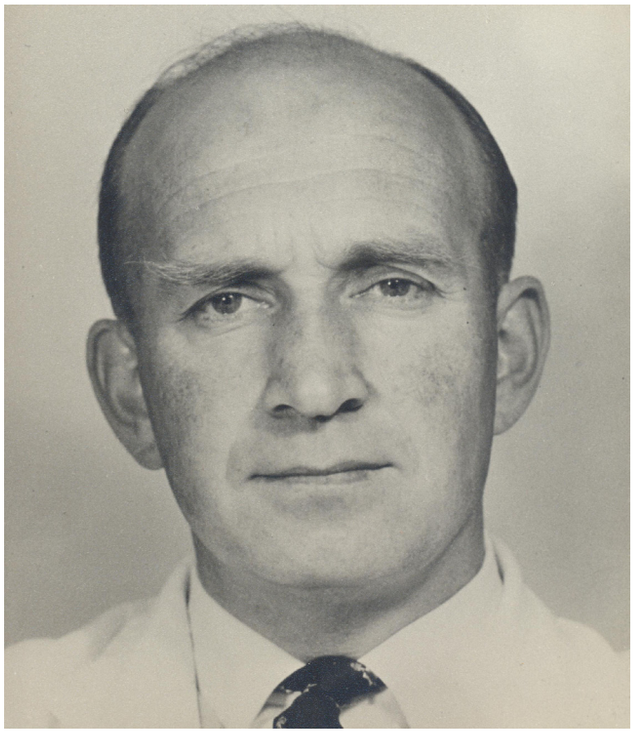

*Fig 4*. James Wilson Millen, MD, DSc (Queen's), ScD (Cantab), 1915-66, photograph reproduced by permission of the Master and Fellows of St. John's College, Cambridge. JWM was Demonstrator, Lecturer then Senior Lecturer in Anatomy, Queen's University, Belfast; Demonstrator, Lecturer then Reader in Anatomy, Cambridge University. My tutor in Anatomy, Clare College, Cambridge, 1952-55, JWM was born in Bangor, Co. Down. In 1932, having been Head Boy at Bangor Grammar School, he became a medical student at Queen's and Malcolm Clinical Scholar. Resident posts followed at the Royal Victoria Hospital. From 1941-48 the two lecturers under Professor Thomas Walmsley were Millen and RH Hunter, Founding Editor of this Journal[20,31]. Millen, in 1944, was appointed Medical Registrar for Queen's University and thus, ex officio, a member of all faculty committees. From 1945-47 he was President of the Queen's University Rugby Football Club[32,33].

suggested the cause was a less than optimal vitamin A intake, supposedly due to adherence to regulations.

During the years 1941-43, consumption of the United States Armed Forces C and K rations led to symptoms of vitamin deficiency[7,29]. This was corrected by McCollum's appointment in 1941 to the US Committees on Nutrition in Defense and Coordination of Information on Food and Nutrition[7]. These appointments were known at Musgrave Park. My father was thus enabled to contact Whitehall and Washington that his food control discrepancies were aimed at preventing vitamin A deficiency. The jaundice epidemic in the US troops in Ulster started[10]. For several weeks the possibility of vitamin A deficiency exacerbating the jaundice led to my father being cleared of wrong-doing. My sister and I were, thereafter, not allowed to eat bananas in public.

## MILLEN AND CAMBRIDGE

When I arrived at Clare College, Cambridge for the Michaelmas Term in 1952, James Wilson Millen (Fig. 4) was assigned as my Anatomy Supervisor. We met weekly for an hour or more for three years. Millen's chief thrust was that anatomy was not useful knowledge without knowing form, function and integration in man and other animals from amoeba up the phylogenetic tree. Millen knew I had been in Belfast from 1940-42[2,9,10]. I knew he had been the other lecturer to Dicky Hunter from 1941 until he came to Clare in1948 via a short stop in Professor Sir Wilfred LeGros Clark's Oxford Department of Anatomy[33]. I also knew that Dicky Hunter was a great and long-time friend of my hero Benjamin Rycroft[9]. Millen's starter reading list was Hamilton, Boyd and Mossman's *Human Embryology,* 2nd edition[34], an edition of Millen and Hunter's Belfast boss, Professor Thomas Walmsley's[35] *Elements of Anatomy*[36] and *Cunningham's Manual of Practical Anatomy*, eleventh edition, revised by JC Brash[37]; four authors of the six, Queen's Belfast or Trinity College Dublin (TCD). In October 1952, Millen said he had heard via Rycroft that his Musgrave Park boss Angus thought that surgeons' children should learn to read using Gray's *Anatomy*. Which edition had I learned on? The correct answer, which I had to look up back in my rooms in Clare Memorial court, was the 18th, 1913, edited by Robert Howden, Professor of Anatomy in the University of Durham. The copy which I still have is inscribed, "Mr. Martin, not to be removed from Wards 5 and 5A"[38]. In 1953 Millen suggested I read McCollum's *Newer Knowledge of Nutrition,* 1929, about the vitamin A and D discoveries[6]. Then we read JH Biggart's *Pathology of the Nervous System*[39] and the *Lancet* galleys of Millen's papers on Vitamin A deficiency and the production of hydrocephalus[40,41] and other neurological malformations. Millen became well-known[42-50]. Soon after I went down to Bart's, Millen went down the Backs as Johnian Praelector and Reader in Anatomy in the University of Cambridge[33].

*Fig 5*. The Carnegie Institution of Washington, Department of Embryology, 1929, photograph of departmental working scientists courtesy of the Alan Mason Chesney Medical Archives of the Johns Hopkins Medical Institutions.From left: Warren H Lewis, George L Streeter, the director since 1918, Martin Nordmann, Emanuel Fauré-Fremiet, Zygmunt Grodzinski, RH "Dicky" Hunter, later founding editor of the *Ulster Medical Journal* and long-time Secretary of Queen's University, Chester H Heuser, Carl G Hartman and Otto Leif Tinklepaugh. This Department and Institution constituted a separate legal entity adjacent to the Johns Hopkins Hospital campus[60].

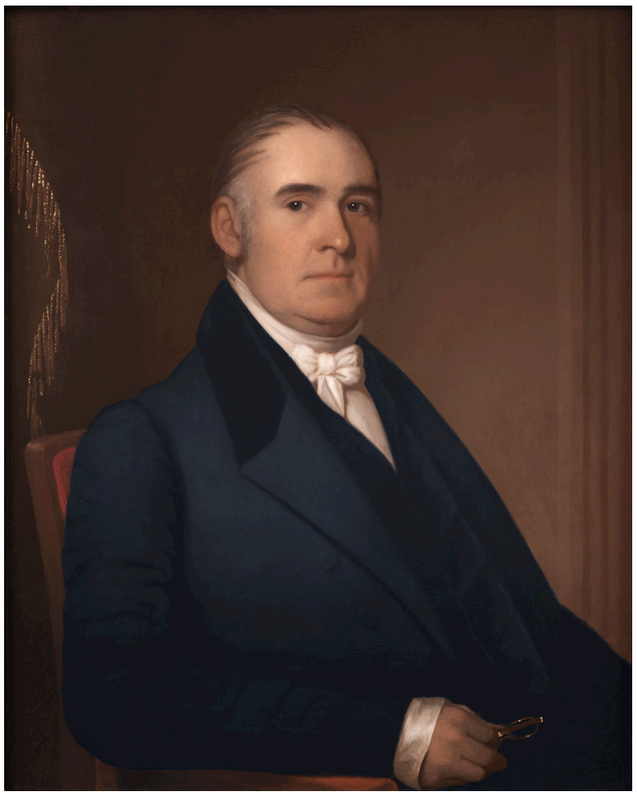

*Fig 6*. Robert Garrett, 1783-1857, oil on canvas, artist unknown. Reproduced courtesy of the Evergreen Museum and Library, Johns Hopkins University Museums.
On February 28, 1827, at the instigation of Robert Garrett, and other Baltimore businessmen the Act of Incorporation of the Baltimore and Ohio Railroad (B and O) was passed by the Maryland Legislature[66]. In 1830, on the B and O, Tom Thumb one-ton locomotives started replacing horses. By 1834 Grasshopper four-wheeled vertical boiler engines had become standard. In the 1840s, Garrett and B and O interests melded, and the Garretts promoted, sold and bought B and O stock. Robert's eldest son Henry was elected to the B and O Board in 1852. In 1854, second son John W Garrett was elected a director. On a 16-14 vote sponsored and promoted by Johns Hopkins, a bachelor, he became president of the B and O in 1858 and served as the first Garrett B and O Railroad president until his death in 1884[64,65].

*Fig 7*. Mary Elizabeth Garrett, 1854-1915, by John Singer Sargent, oil on canvas, 1904, unveiled October 4, 1904, in the rotunda of the Johns Hopkins Hospital. Courtesy of the Alan Mason Chesney Medical Archives of the Johns Hopkins Medical Institutions, photograph by Aaron Levin.
Grand-daughter of Lisburn-born Robert Garrett, Mary Elizabeth was her father John W Garrett's only daughter and amanuensis. As such she became an eminencée grise of the Baltimore and Ohio Railroad[65] whose stock climbed from 50 to over 170 during her father's presidency[66]. The will of Johns Hopkins, who died on Christmas Eve 1873, left a seven million dollar estate, $130 million today, to found a University. Johns Hopkins's Baltimore and Ohio shares were over half the estate. Half the shares were deeded to maintain the University without encroaching on the capital of the shares. The other half of Johns Hopkins's estate was willed to found the Johns Hopkins Hospital[65]. Mary, in 1884 inherited from her father to become the wealthiest spinster in America[65] and a past-master of coercional philanthropy. She gave to Johns Hopkins School of Medicine and the Hospital on condition that women be admitted on the same terms as men and that the school be graduate level. William H Welch[18] was enabled by the Garrett gifts to become the first Professor of Pathology, a eulogist at Miss Garrett's Memorial Service in 1915[65] and the teacher together with Rich, his subsequent successor, of John Henry Biggart, who in 1931-32 was on a Harkness Fellowship from Queen's University Belfast[21].

When I started experimental studies, Millen's teaching on the necessity to control the milieu interieur of experimental animals was invaluable[51]. His teaching on the use of electron microscopy in biology aided my research colleagues when we studied the blood-brain barrier[52,53] and the lung and haemoglobin[54-58]. Millen's monograph on the cerebrospinal fluid with his long-time collaborator David Woollam, also a great teacher, was a most useful reference[59].

I asked Dr Millen why Queen's Belfast graduates had such leading roles in Teratology, Embryology and Applied Anatomy. Millen replied Dicky Hunter and Hopkins (Fig. 5). I thought he meant Gowland, not Johns. Millen politely suggested I read Gowland Hopkins's 1929 Nobel Oration[23] as well as his now classic 1906 address to the Society of Public Analysts[61], and George L Streeter's recent posthumously published *Apologia pro vita mea*[62]. Millen regretted he had not gone to Hopkins from Queen's like Hunter, Biggart and Boyd, but at least we were working next to the Hopkins building for Biochemistry at Cambridge. Millen also introduced me to his collaborators in Sir Joseph Barcroft's adjacent Physiology department. Millen had worked with Sir Joseph Barcroft's son Henry when they were both at Queen's. Henry got his FRS in 1953. I was also introduced to the biochemists in Francis Young's Department in the Hopkins Building.

 


*Fig 8*. Winston S Churchill and President Harry S Truman wave from the special Baltimore and Ohio train on their way to Westminster College, Missouri. From the Collections of the B & O Railroad Museum, Baltimore, Maryland. They "exchanged information about the American Civil War as they looked at the West Virginia and Maryland sites of famous battles…The discussion started when Mr Truman told Mr. Churchill their train was passing through Harpers Ferry. 'I know' Mr Churchill said, 'that's where Jackson seized McClellan's stores'. Mr Churchill also recounted how he had motored through Frederick, Maryland with the late President and Mrs. Roosevelt and Harry Hopkins en route to "Shangri-La"[67]. Harry Hopkins, also on the B and O train, confirmed the details of that war time journey.

## THE LISBURN GARRETTS

On the 10th April 1790, Robert Garrett sailed from Belfast on the American-owned brig, the *Brothers*[63]. Born near Lisburn, County Down, on the 2nd May, 1783, Robert was the youngest of the six children of John and Margaret MacMechen Garrett[64,65]. The family arrived in Wilmington, Delaware in May 1790. His father died on the voyage or soon after but his mother was able to buy a farm in Cumberland County, Pennsylvania. As a Scottish Calvinist mother, she worked the family hard[66]. At sixteen, Robert wintered with Ohio Indians. In 1801 he first visited Baltimore, Maryland. By 1814, Wallace and Garrett was prospering. He dissolved the partnership on the death of his first wife, Martha, but married in May 1817 Elizabeth Stouffer, daughter of a Baltimore merchant. By 1819 Robert Garrett and Company were doing business with the rest of the United States and the British Empire.

The family of Robert Garrett Senior rescued Johns Hopkins Medical School and enabled its Hospital to be completed after the crash of 1873 - a rail-road financial bubble from which it took the US economy a decade to recover[65]. The B and O and Johns Hopkins were saved by Robert Garrett's (Fig 6) son and grand-daughter (Fig. 7) travelling to London and raising over $200 million in today's money from Barings just prior to the crash[66]. That was what Winston Churchill told us on 7th December 1951[10] when we dined with him, and we Harrow Monitors discussed the American Civil War. In response to a question about his 1946 Fulton, Missouri trip on the B and O, Churchill (Fig. 8) said Harry Truman was "an astute card player who had won my money." "Never criticize the office of the President of the United States. Remember, young men, he is Commander-in-Chief".

The New York Times had a slightly different take on the journey. Along the main line of the B and O the route passed many Civil War sites. Churchill was known to be extremely knowledgeable[67] about this horrendous first modern war in which 630,000 were killed[68]. President Truman and his military aides were taught much. After his Iron Curtain speech at Westminster College[69], Churchill took his B and O Railroad carriage back to Washington, stopping en route to visit Civil War memorials. Truman and his entourage flew back sans Winston[69] and his mother Jennie Jerome's stories of the Garrett boys: in the Athens Olympic Games of '96, Robert Garrett III was the winner of both the discus throw and the shot put. He placed second in the high jump and the long jump. For each first place medal he received an olive branch and for each second place medal a branch of laurel, along with their respective diplomata[70].

## POSTSCRIPT

Sir Frederick Gowland Hopkins in his 1929 Nobel lecture asked "Who was the 'discoverer' of vitamins? This question has no clear answer. So often in the development of science, a fundamental idea is foreshadowed in many quarters but has long to wait before it emerges as a basis of accepted knowledge". He continued, "…The work and words of true pioneers lay forgotten because published when average minds were not ready to appraise them at their right value" [23].

Winston Churchill, not a Hopkins "average mind", told us on the 7th December 1951[10] that he had in March 1946 fulfilled a boyhood ambition. He had deployed his B and O coach on the return to Washington, DC like George Brinton McClellan or Robert E Lee*. Churchill had looked for signs of Stonewall Jackson's extensive destruction: he had been told of the Garretts' heroic reconstruction efforts and their saving endowment of the Hopkins.

In the continuing focus of interest in Vitamin A and the dramatic public health improvements with its deployment by the World Health Organization[71,72], Johns Hopkins continues the path of Elmer V McCollum, Gowland Hopkins and JW Millen[73] (Fig. 9).

### ACKNOWLEDGEMENT

Thanks are due to Mr James R Garrett, President, Evergreen House Foundation, Baltimore, MD, and to the staff of the US Library of Congress, Manuscript Division for permission to examine the *Robert Garrett Family Papers.* Container No. 1 has two communications dated 17th October and 8th November 1782, written and signed by Charles Carroll of Carrollton, who, on Independence Day 1828, aged 90, as the sole surviving signatory of the 1776 Declaration of Independence, laid the Cornerstone of the B & O Railroad. The authors have no conflict of interest.

* General McClellan, former President of the Ohio and Mississippi Railroad, was a life-long close friend of the Garretts, despite being fired after the September 1862 battle at Antietam, MD[65,66], by President Lincoln and John W Garrett. John W Garrett's son, Robert Garrett II, succeeded General Robert E Lee, on Lee's death in 1870, as President of the Valley Railroad, a B and O subsidiary. In 1863 Robert Garrett II had escaped through Union barricades to join Lee's Confederate Army of the North Potomac[65].

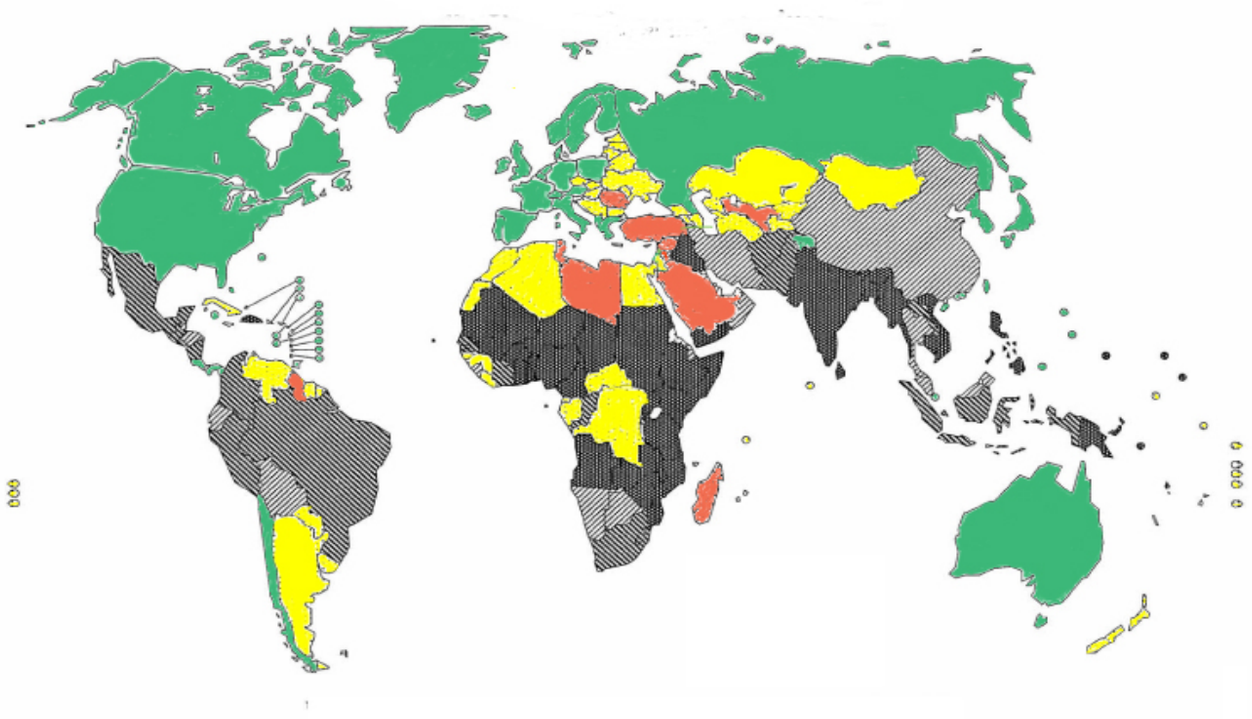

*Fig 9*. Countries categorized by degree of public health importance of vitamin A deficiency

Clinical
Severe; subclinical
Moderate; subclinical
Mild; sporadic or high-risk
No data; problem likely
Problem under control

This World Health Organization (WHO) map[74] does not purport to show current political boundaries, but does delineate the world-wide prevalence of Vitamin A deficiency. More current information is available from WHO[72] and from the recent review authored by the former Dean of the Michael R Bloomberg School of Public Health of Johns Hopkins University[73]. The underlying cause of the vitamin A deficiency is an inadequate diet, for example, the United States Armed Forces reliance on C and K rations during the years 1941-43[29].

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